

REMARKS

By the present amendments, claim 5 has been cancelled and the subject matter thereof has been incorporated into claim 1. To accord with this change, other claims (i.e. claims 2, 3, 4, 39 and 41) have been amended to revise claim dependencies and to ensure that recited terms have proper antecedents.

Claim 14 has been revised to recite C8-C16 alkyl benzene sulfonic acids and not merely alkali metal, alkaline earth metal, ammonium or alkylamine salts thereof. Support for this amendment can be found throughout the specification. See, for example, original claim 17 and page 3, line 20 of the present specification wherein alkyl benzene sulfonic acids are expressly recited. See also page 3, line 20-21 and Composition II at bottom of page 10 of the present specification, wherein dodecyl benzene sulfonic acid is expressly recited. It would be obvious to the person skilled in the art reading the entire specification that the applicants intended to include the acid form of these compounds within the scope of the invention. Corresponding amendments have been made to the specification, as noted above.

New claim 42 has been added and is directed to a multi-component system which can be combined to provide a disinfecting solution according to claim 1. Support for this amendment can be found at page 4, line 19-22 of the present specification. See also Example X, at page 29 which exemplifies a two-part liquid system.

A comma has been removed from claims 38-41 to make them consistent with the other claims.

Throughout the specification, claims and abstract, the term "diphenyl sulfonate" has been replaced with the narrower and more accurate term ---diphenyl oxide sulfonate---. Support for this amendment can be found throughout the specification. See, for example, page 7, line 13 and page 23, line 18-21. See also original claim 18.

With the entry of the present amendments, claims 1-4, 6-33 and 38-42 will be pending and claim 5 will be cancelled. Claims 34-37 are withdrawn from consideration.

Applicants also wish to thank Examiner Schlientz and his supervisor Johann Richter for granting a personal interview on June 20, 2007. This response is prepared in accordance with the interview summary of same date, and particularly the submission of comparative data showing that the alleged closest prior art, i.e., Example 3 of Beilfuss, does not show sporicidal activity.

The rejections of the Examiner will now be addressed below under the appropriate headings.

35 U.S.C. §§ 102 and 103

All claims stand rejected for being anticipated or obvious in view of at least one of International Publication No. WO 99/52360 to Serego Allighieri et al. (Allighieri), U.S. Patent No. 5,387,605 to Beilfuss et al. (Beilfuss), U.S. Patent No. 6,309,470 to Schulhoff et al. (Schulhoff), U.S. Patent No. 5,900,256 to Scoville, Jr. et al. (Scoville), and EP Patent No. 0 351 772 to McMillen (McMillen). Included in the rejections is a rejection of Claim 5 for being obvious in view of Allighieri taken in combination with Beilfuss.

As a result of the present amendments, claims 1 and 5 have been combined into amended claim 1. This claim has been further amended to be directed to a **sporicidal solution**. Claim 1 is reproduced below:

1 (Currently amended). An aqueous mycobactericidal and **sporicidal solution** having a pH of from 0.6 to 7 and comprising:

- (a) hydrogen peroxide in a concentration of from 0.01 to 6% w/w, based on the total weight of the solution; and
- (b) 2-furan carboxylic acid in a concentration of from 0.01 to 8% w/w, based on the total weight of the solution.

[emphasis added]

The remaining claims are each dependent, either directly or indirectly, on amended claim 1 and therefore incorporate all its limitations.

Applicants respectfully submit that the invention claimed in amended claim 1 is not obvious for the following reasons.

As indicated in the accompanying Affidavit of Navid Omidbakhsh dated July 18, 2007, flexible endoscopes are used in invasive medical procedures and therefore must be disinfected using a disinfectant that has, amongst other things, mycobactericidal and sporicidal activity. They are also heat sensitive and therefore only chemical disinfectants can be used.

It is known in the disinfection industry that hydrogen peroxide based solutions are not compatible with flexible endoscopes as they tend to either damage them and reduce their useful life, or are ineffective in achieving the level of disinfection that is required.

The only disinfectants in current use that are not corrosive to flexible endoscopes and which are effective in high level disinfection and sterilization are those containing aldehydes. Aldehydes are toxic and noxious to users and a need exists for alternative formulations that are effective, non-toxic, and which will not damage sensitive medical instruments such as flexible endoscopes.

Hydrogen peroxide is non-toxic and user- and environmentally-friendly as the breakdown products are oxygen and water. However, commercial solutions tend to be ineffective in achieving the level of disinfection that is required or are damaging to sensitive medical instruments (e.g. flexible endoscopes).

To date, to the best of the Applicants' knowledge, no company has developed a hydrogen peroxide based disinfectant that has mycobactericidal and sporicidal activity and that is compatible with flexible endoscopes. Commercial hydrogen peroxide based disinfectants rely on hydrogen peroxide concentrations of 7 w/w % or higher which are damaging to such instruments.

Despite the failure of others, the Applicants have succeeded in developing a low-volatility, low toxicity, non-corrosive, non-irritating, and stable aqueous sporicidal and mycobactericidal solution that is compatible with flexible endoscopes. See, for example, page 5, line 23, wherein the present specification states that a "major field of application is in the processing of delicate surgical instruments and devices, including flexible endoscopes." See also page 21, line 16-20 (Example III), wherein Composition II was tested under conditions which simulated conditions present in an endoscope processing machine. See also page 1, line 7 to page 2, line 12 and page 5, line 2-15 of the present specification.

As stated in the present specification at page 6, line 28-30, 2-furan carboxylic acid has been described as possessing some bactericidal, fungicidal and mycobactericidal activity, particularly when formulated in combination with traditional mycobactericidal ingredients. The present invention resides in the combination of this compound with hydrogen peroxide in specified concentrations and pH to provide a surprisingly effective mycobactericidal and sporicidal solution that is compatible with sensitive medical devices. See, for example, page 2, line 15-16 of the present specification.

The present invention provides solutions which are a dramatic improvement over existing hydrogen peroxide disinfectants. Contact times in high level disinfection may be reduced by factors of up to 4-5 using hydrogen peroxide concentrations which are lower by as much as one

order of magnitude compared to prior art solutions (see page 5, line 16-19 of the present specification).

The following categories of microorganisms are listed below in terms of difficulty of kill, with bacterial endospores being the most difficult to kill and enveloped viruses the easiest to kill:

bacterial endospores (or simply spores)

mycobacteria

fungi

non-enveloped viruses

bacteria

enveloped viruses

Solutions according to the invention containing hydrogen peroxide in a concentration as low as 2 w/w % can be used to inactivate spores and mycobacteria present on sensitive medical instruments, such as flexible endoscopes, without damaging them. The Applicants conducted internal tests in which they put flexible endoscopes through 1000 cycles in an endoscope processing machine using a solution according to the present invention and determined that no damage resulted. The solution tested is summarized in TABLE 1 below:

TABLE 1

Raw material	Percent (w/w%)
deionized water	Qs to 100
1-hydroxyethylidene-1,1-diphosphonic acid	0.9
phosphoric acid	1.5
dodecylbenzene sulfonic acid	0.18
C6-diphenyl oxide disulfonate	0.07
2-furan carboxylic acid	1.0
C10-linear alcohol ethoxylate (3.5 moles of ethoxylated, average)	0.05
hydrogen peroxide	2.0
caustic potash	Up to pH=2.5

Publication No. WO 99/52360 to Serego Allighieri et al. (Allighieri) and U.S. Patent No. 5,387,605 to Beilfuss et al. (Beilfuss) do not teach or suggest an antimicrobial solution compatible with sensitive medical devices, especially flexible endoscopes. These references also

do not teach solutions that have enhanced mycobactericidal and sporicidal activity.

Allighieri

Allighieri teaches disinfecting solutions for use on hard surfaces such as those present in a household (e.g. see bottom of page 22 to top of page 23; page 3, second paragraph; page 9, second last paragraph; page 10, last paragraph; and page 11, first two paragraphs).

The invention of Allighieri is based on a finding that a specifically defined poly(alkylene glycol) alkyl ether imparts immediate and long lasting disinfecting performance and cleaning properties to a solution containing a disinfecting material (e.g. page 2, third full paragraph from top). The solutions are stated to provide broad spectrum activity against Gram negative and Gram positive bacterial strains (page 2, last paragraph). See also page 7, second full paragraph wherein a variety of bacteria against which the invention is effective are named. None of the bacteria are spores. **No effectiveness against spores is suggested, demonstrated or claimed.**

Essential ingredients of solutions according to the Allighieri invention are a disinfecting material and certain defined poly(alkylene glycol) alkyl ethers. All other recited ingredients are stated to be optional. Apart from the poly(alkylene glycol) alkyl ether, all ingredients disclosed in this reference are employed for their well known properties.

The disinfecting material can be “any known ingredient having the ability of reducing or even eliminating [*sic*] by killing the microorganisms existing on a surface” (page 3, last full paragraph). Such material includes “all those known by those skilled in the art for the purpose of disinfecting and may include bleaches, like peroxygen bleaches and/or chlorine-type bleaches; antimicrobial essential oils or actives thereof; quaternary ammonium compounds; phenolic compounds; aldehydes like glutaraldehyde, formaldehyde, glyoxal; parabens like ethyl paraben, propyl paraben, methyl paraben; organic acids and peroxy acids; alcohols; and mixtures thereof (page 4, first full paragraph).

The specification contains a long list of disinfecting materials that can be used in the compositions. Suitable anti-microbial essential oils and their actives are discussed starting at page 5, fourth full paragraph. Suitable quaternary ammonium compounds are discussed starting at page 6, fourth full paragraph. Suitable phenolic compounds are discussed at bottom of page 6. Other suitable disinfecting materials include chlorine-type bleaches like hypochlorite (page 7, first paragraph).

Optional ingredients include **any** surfactant known to those skilled in the art such as

anionic, nonionic, cationic, amphoteric and/or zwitterionic surfactants. The surfactants are used to contribute to the cleaning performance of the disinfecting compositions and not to enhance the level of disinfecting activity (page 11, last full paragraph).

As in the case of the disinfecting material, Allighieri recites an extremely long list of examples of suitable surfactants starting at the bottom of page 11 and ending near the top of page 17.

Long lists of other optional ingredients are recited including chelating agents (page 17, 2nd full paragraph onwards), radical scavengers (page 18, near bottom of page onwards), solvents (page 19, second full paragraph onwards), pH buffers (page 20, first full paragraph onwards), builders, stabilizers, bleach activators, soil suspenders, dye transfer agents, brighteners, perfumes, anti dusting agents, enzymes, dispersants, dye transfer inhibitors, pigments, perfumes and dyes.

The number of possible combinations of recited ingredients is extremely high. Moreover, there is no teaching of incorporating 2-furan carboxylic acid into solutions according to the invention.

Beilfuss

Beilfuss teaches solutions for use in the general disinfection of surfaces, instruments, appliances, skin and hands and contains no specific teaching of disinfection of sensitive medical instruments such as flexible endoscopes (e.g. column 4, line 41-50). While the solutions of Beilfuss are shown to inactivate mycobacteria, longer contact times are required to achieve the same level of disinfection as can be achieved by the present inventive solution. For example, at column 5, EXAMPLE 2 shows that a solution containing 2-furan carboxylic acid in a concentration of 0.5 w/w % takes 30 minutes to inactivate mycobacteria. In contrast, Composition I (containing 0.5 w/w % of 2-furan carboxylic acid and 0.5 w/w % hydrogen peroxide) is effective in inactivating mycobacteria in a contact time of only five minutes. (see page 20, Table 10 of the present application).

See also Table II (page 21) of the present application wherein test results show a 0.50 w/w % solution of hydrogen peroxide to be ineffective in killing mycobacteria in a contact time of five minutes and that a 0.50 w/w % solution of 2-furan carboxylic acid is likewise ineffective. However, a combination of hydrogen peroxide and 2-furan carboxylic acid, each present in a concentration of 0.50 w/w % (Composition I), leads to a greater than 5 log reduction in

mycobacteria in a contact time of five minutes.

Example III of the present application also demonstrates the synergy between H₂O₂ and 2-furan carboxylic acid, as the other ingredients of Composition II (disclosed at page 11, line 11 onwards) are merely corrosion inhibitors (Cobratec 99, sodium molybdate, sodium nitrite), a buffer (sodium carbonate) and tap water.

The present specification contains other examples showing the effectiveness of the present invention in killing a wide range of test organisms, including spores (e.g. *Bacillus subtilis*). Sporicidal activity is demonstrated in Example III (Composition II; page 21, line 16 to page 22, line 10), Example X (Solutions P or Q; page 29, line 3 onwards) and Example XI (Solution R; page 30, line 2 onwards).

The synergy between hydrogen peroxide and 2-furan carboxylic acid is quite unexpected. While Beilfuss teaches that hydrogen peroxide may be combined with 2-furan carboxylic acid to increase the spectrum of activity (column 3, line 10-18), there is no teaching that combining these ingredients would lead to an enhancement of disinfecting activity against mycobacteria or spores. Indeed, Beilfuss teaches that the combination of two biocidal ingredients may not lead to any enhancement of activity. For example, see column 6, line 25-30 wherein Beilfuss states, “The example shows that the combination of carboxylic acid according to the invention with other biocidal active ingredients such as benzalkonium chloride is as effective as before against Tb, whilst a combination with acids, for example, phosphoric acid does not develop any efficacy against Tb.”

To verify that Beilfuss does not teach sporicidal solutions, one of the Applicants, Navid Omidbakhsh, tested the solution of Example 3 of Beilfuss for sporicidal activity. The solution tested is summarized below in Table 2.

Table 2: Beilfuss Solution (Example 3)

Ingredient	% w/w (based on total weight of solution)
Deionized water	96.50
Benzalkonium chloride	2.50
Furoic acid	1.00

The Beilfuss Solution was tested using the Quantitative Carrier Test Method I against *Bacillus subtilis* and the results are shown in Table 3 below.

Table 3: The activity of the Beilfuss Solution against *B.subtilis* (QCT 1)

Repeats	Dilution	Contact Temp	Contact Time	Average Log ₁₀ Red'n
3	Full strength	RT	15 min	less than 0.3
3	Full strength	50°C	15 min	less than 0.3
3	Full strength	RT	6 hours	less than 0.3

The results demonstrate that the Beilfuss solution of Example 3 containing 2.5 w/w % benzalkonium chloride (i.e. 10 pts at 25% dilution) and 1 w/w % 2-furan carboxylic acid (i.e. 2 parts at 50% dilution) **does not** have sporicidal activity.

Given the teachings of Beilfuss and Mr. Omidbakhsh's above experiment, the person skilled in the art would not be able to predict or have a reasonable expectation of success that even a mere additive effect would arise by combining two or more biocidal ingredients. It would therefore not be obvious to the person skilled in the art, reading Beilfuss alone or in combination with Allighieri, that a synergistic mycobactericidal and sporicidal solution, effective at short contact times, would result from a combination of 2-furan carboxylic acid with another active ingredient (e.g. hydrogen peroxide). In addition, any allegation of obviousness based on the combination of Allighieri and Beilfuss is effectively rebutted by the comparative evidence set forth in the specification and Tables 1-3 discussed above. The results of the additional testwork are also found in the attached Affidavit.

Non-statutory obviousness-type double patenting – US 6,803,057

The Examiner has rejected claims 1-33 on the ground of non-statutory obviousness-type double patenting as being unpatentable over claims 19 and 20 of U.S. patent no. 6,803,057.

Applicant respectfully traverses this rejection. As amended, all claims require the presence of 2-furan carboxylic acid, a monocarboxylic acid. Examiner states that this compound is an obvious variant of monocarboxylic acid claimed in the '057 Patent but has not provided any reasons in support of this contention.

Applicants submit that the approach governing obviousness determinations under 35 U.S.C. 103 applies equally to double patenting determinations. Regarding obviousness determinations under 35 U.S.C. 103, MPEP section 2144.08 states,

[the] patentability of a claim to a specific compound or subgenus embraced by a prior art genus should be analyzed no differently than any other claim for purposes of 35 U.S.C. § 103....The fact that a claimed species or subgenus is encompassed by a prior art genus is not sufficient by itself to establish a *prima facie* case of obviousness. *In re Baird*, 16 F.3d 380, 382, 29 USPQ2d 1550, 1552 (Fed. Cir. 1994)...; *In re Jones*, 958 F.2d 347, 350, 21 USPQ2d 1941, 1943 (Fed. Cir. 1992) (Federal Circuit has "decline[d] to extract from *Merck [& Co. v. Biocraft Laboratories Inc.*, 874 F.2d 804, 10 USPQ2d 1843 (Fed. Cir. 1989)] the rule that... regardless of how broad, a disclosure of a chemical genus renders obvious any species that happens to fall within it."). See also *In re Deuel*, 51 F.3d 1552, 1559, 34 USPQ2d 1210, 1215 (Fed. Cir. 1995).

To establish a *prima facie* case of obviousness, it is essential that Office personnel find some reason to make the claimed invention in light of the prior art teachings. See *KSR International Inc., v. Teleflex Inc.*, 127 S. Ct. 1727; April 30, 2007.

As the Examiner has not pointed out any reason to select 2-furan carboxylic acid from the class of monocarboxylic acids, Applicants submit that the Examiner has not met his burden of establishing a *prima facie* case of obviousness-type double patenting.

As discussed above, the combination of 2-furan carboxylic acid with hydrogen peroxide is surprisingly and unexpectedly effective and provides a solution that is effective as a mycobactericide and sporicide. Applicants' arguments above in support of the non-obviousness of the claimed invention in view of the cited prior art apply also here to overcome the double patenting rejection based on the '057 Patent.

Provisional non-statutory obviousness-type double patenting – US 11/518,188

Claims 1-6, 14-22, 27 and 30-33 stand provisionally rejected on the ground of non-statutory obviousness-type double patenting as being unpatentable over claims 24-32, 34-35, 37-46, 48-49 and 51 of co-pending application no. 11/518,188.

As amended, the claims all require the presence of 2-furan carboxylic acid. This compound is not recited in any of the cited claims of the co-pending application. However, claim

37 recites a disinfecting solution comprising, amongst other things, “at least one additional ingredient chosen from monocarboxylic acid.” Thus, the reasons given above to overcome the double patenting rejection based on US 6,803,057 apply equally here. That is, by not citing any motivation or suggestion to select 2-furan carboxylic acid from the class of monocarboxylic acids, the Examiner has not met his burden of establishing a *prima facie* case of obviousness-type double patenting. The fact that a claimed species or subgenus is encompassed by a prior art genus is not sufficient by itself to establish a *prima facie* case of obviousness. In any event, the invention as a whole is not obvious in view of the subject matter claimed in the cited co-pending application for the reasons given above.

Provisional non-statutory obviousness-type double patenting – US 11/128,223

Claims 1-22, 27 and 30-33 are provisionally rejected on the ground of non-statutory obviousness-type double patenting as being unpatentable over claims 1, 3-6, 8-11, 15-16 and 18-19 of co-pending application no. 11/128,223.

The cited co-pending application was filed May 13, 2005. In contrast, the present application was filed earlier, i.e. on November 17, 2003. Consequently, there can be no improper time-wise extension of the patent term of the **present application**. Applicant respectfully submits that any double patenting rejection that is raised should be raised against the co-pending ‘223 application.

In any event, the cited claims of the ‘223 are not obvious in view of the subject claims of the present application. Examiner will see that the cited claims of the ‘223 application all require the presence of “at least one surfactant chosen from imidazoline derivatives, alkyl betaines, alkyl amidopropyl betaine amides, alkyl amidopropyl betaines, alkylsulfo betaines, amine oxides and derivatives thereof in a concentration of from about 0.01 to about 15% w/w of the solution” (claims 1-17) or “at least one surfactant chosen from alkyl betaines, alkyl amidopropyl betaines, alkyl amidopropyl betaine amides, alkylsulfo betaines, alkyl amphocarboxylates, alkyliminocarboxylates, amine oxides and derivatives thereof in a concentration of from about 1 to about 5% w/w of the solution” (claims 18-20). As these compounds are not disclosed in the present application or in any other prior art reference cited by the Examiner, the Examiner has not made out a *prima facie* case of obviousness.

Request for Withdrawal of Restriction Requirement

Currently, claims 34-37 are withdrawn from consideration as being drawn to a different invention. Applicants submit that since claim 1 has been shown to be patentable over the applied prior art, Applicants should be entitled to also claim the patentable composition in terms of a dry particulate composition dissolvable in water as defined in claims 34 and 35. Similarly, since the method of cleaning equipment as defined in claim 36 uses the patentable solution of claim 1, this method is equally patentable and the restriction requirement for this claim as well as its dependent claim 37 should be withdrawn as well.

Claim 42

It is also submitted that claim 42 is proper for inclusion into the application. While claim 42 characterizes the composition in a multi-component form, this claim still incorporates the patentable aspect of the composition of claim 1 through its dependency and it should be allowed along with remaining claims.

Information Disclosure Statement

It is noted that the "Other References" in the Information Disclosure Statement filed on October 22, 2004 were not initialed by the Examiner. No mention was made in the Office Action regarding these references, e.g., copies cannot be located, so it is assumed that this was an oversight on the part of the Examiner. Thus, the Examiner is respectfully requested to return the Information Disclosure Statement showing that these references have been considered.

SUMMARY

In light of the amendment to claim 1, the attached Affidavit, and the arguments set out above, it is submitted that any *prima facie* case of obviousness that may have been established by the combination of Allighieri and Beilfuss has been effectively rebutted. The comparative evidence in the specification coupled with the additional evidence submitted in the Affidavit shows that the combination of components of claim 1 provides unexpected benefits in terms of mycobactericidal and sporicidal activity. In light of this evidence, all pending claims are now in condition for allowance.

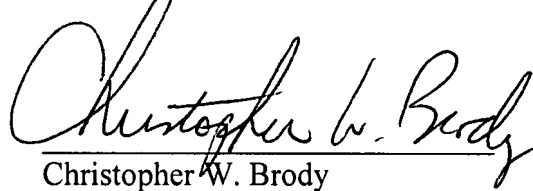
If the Examiner believes that an additional interview with Applicants' attorney would be

helpful in expediting prosecution of this application, the Examiner is respectfully requested to telephone the undersigned at 202-835-1753.

Again, reconsideration and allowance of this application is respectfully requested.

A petition for a one month extension of time is hereby made. A check in the amount of \$170.00 is submitted herewith for the extension of time fee (\$120.00) and 1 new extra claim (\$50.00). Please charge any additional fee deficiency or credit any overpayment to Deposit Account No. 50-1088.

Respectfully submitted,
CLARK & BRODY

A handwritten signature in cursive script, reading "Christopher W. Brody", written over a horizontal line.

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